09/869136

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NEWS 2	Apr 08	"Ask CAS" for self-help around the clock
NEWS 3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4	Apr 09	ZDB will be removed from STN
NEWS 5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS 15	Jul 30	NETFIRST to be removed from STN
NEWS 16	Aug 08	CANCERLIT reload
NEWS 17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18	Aug 08	NTIS has been reloaded and enhanced
NEWS 19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
NEWS 24	Sep 16	Experimental properties added to the REGISTRY file
NEWS 25	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 26	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 27	Oct 21	EVENTLINE has been reloaded
NEWS 28	Oct 24	BEILSTEIN adds new search fields
NEWS 29	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 30	Oct 25	MEDLINE SDI run of October 8, 2002
NEWS 31	Nov 18	DKILIT has been renamed APOLLIT
NEWS 32	Nov 25	More calculated properties added to REGISTRY
NEWS 33	Dec 02	TIBKAT will be removed from STN
NEWS 34	Dec 04	CSA files on STN
NEWS 35	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 36	Dec 17	TOXCENTER enhanced with additional content
NEWS 37	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 38	Dec 30	ISMEC no longer available
NEWS 39	Jan 13	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 40	Jan 21	NUTRACEUT offering one free connect hour in February 2003
NEWS 41	Jan 21	PHARMAML offering one free connect hour in February 2003
NEWS 42	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 43	Feb 13	CANCERLIT is no longer being updated
NEWS 44	Feb 24	METADEX enhancements
NEWS 45	Feb 24	PCTGEN now available on STN
NEWS 46	Feb 24	TEMA now available on STN
NEWS 47	Feb 26	NTIS now allows simultaneous left and right truncation

NEWS 48 Feb 26 PCTFULL now contains images

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=> e proft thomas/au
E1          50     PROFT T/AU
E2           1     PROFT T L/AU
E3          35 --> PROFT THOMAS/AU
E4           3     PROFT V/AU
E5           1     PROFT W/AU
E6           1     PROFT WILTRUD/AU
E7           1     PROFUGHI TERENCE C/AU
E8          78     PROFUMO A/AU
E9           1     PROFUMO ALBERTO/AU
E10         10     PROFUMO ALDO/AU
E11         41     PROFUMO ANTONELLA/AU
E12         79     PROFUMO E/AU

=> s e1-e3
L1          86 ("PROFT T"/AU OR "PROFT T L"/AU OR "PROFT THOMAS"/AU)

=> e fraser john d/au
E1          32     FRASER JOHN/AU
E2           1     FRASER JOHN ANGUS/AU
E3          74 --> FRASER JOHN D/AU
E4           2     FRASER JOHN DAVID/AU
E5          11     FRASER JOHN DOUGLAS/AU
E6           2     FRASER JOHN E/AU
E7           3     FRASER JOHN F/AU
E8           6     FRASER JOHN G/AU
E9           1     FRASER JOHN J/AU
E10          4     FRASER JOHN J JR/AU
E11          1     FRASER JOHN JAMES/AU
E12         52     FRASER JOHN K/AU

=> s e3-e5
L2          87 ("FRASER JOHN D"/AU OR "FRASER JOHN DAVID"/AU OR "FRASER JOHN
               DOUGLAS"/AU)

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=> s l1 or l2
L3         156 L1 OR L2

=> s l3 and superantigen
L4          66 L3 AND SUPERANTIGEN

=> s l4 and streptococc?
L5          38 L4 AND STREPTOCOCC?

=> s l5 and smez?
L6          30 L5 AND SMEZ?

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7           9 DUP REM L6 (21 DUPLICATES REMOVED)
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=> d bib ab 1-9

L7 ANSWER 1 OF 9 MEDLINE
AN 2003084097 IN-PROCESS
DN 22483693 PubMed ID: 12595453
TI Two novel superantigens found in both group a and group C **streptococcus**.
AU **Proft Thomas**; Webb Phillip D; Handley Vanessa; **Fraser John D**
CS Department of Molecular Medicine and Pathology, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand.
SO INFECTION AND IMMUNITY, (2003 Mar) 71 (3) 1361-9.
Journal code: 0246127. ISSN: 0019-9567.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030222
Last Updated on STN: 20030222
AB Two novel **streptococcal superantigen** genes (speL(Se) and speM(Se)) were identified from the **Streptococcus** equi genome database at the Sanger Center. Genotyping of 8 S. equi isolates and 40 **Streptococcus** pyogenes isolates resulted in the detection of the orthologous genes speL and speM in a restricted number of S. pyogenes isolates (15 and 5%, respectively). Surprisingly, the novel **superantigen** genes could not be found in any of the analyzed S. equi isolates. The results suggest that both genes are located on a mobile element that enables gene transfer between individual isolates and between **streptococci** from different Lancefield groups. S. equi pyrogenic exotoxin L (SPE-L(Se))/**streptococcal** pyrogenic exotoxin L (SPE-L) and SPE-M(Se)/SPE-M are most closely related to **SMEZ**, SPE-C, SPE-G, and SPE-J, but build a separate branch within this group. Recombinant SPE-L (rSPE-L) and rSPE-M were highly mitogenic for human peripheral blood lymphocytes, with half-maximum responses at 1 and 10 pg/ml, respectively. The results from competitive binding experiments suggest that both proteins bind major histocompatibility complex class II at the beta-chain, but not at the alpha-chain. The most common targets for both toxins were human Vbeta1.1 expressing T cells. Seroconversion against SPE-L and SPE-M was observed in healthy blood donors, suggesting that the toxins are expressed in vivo. Interestingly, the speL gene is highly associated with S. pyogenes M89, a serotype that is linked to acute rheumatic fever in New Zealand.

L7 ANSWER 2 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 2002:513642 BIOSIS
DN PREV200200513642
TI The bacterial **superantigen streptococcal** mitogenic exotoxin Z is the major immunoactive agent of **Streptococcus** pyogenes.
AU Unnikrishnan, Meera; Altmann, Daniel M.; **Proft, Thomas**; Wahid, Faisal; Cohen, Jonathan; **Fraser, John D.**; Sriskandan, Shiranee (1)
CS (1) Department of Infectious Diseases, Faculty of Medicine, Hammersmith Hospital, Imperial College School of Science, Technology, and Medicine, Du Cane Road, London, W12 0NN: s.sriskandan@ic.ac.uk UK
SO Journal of Immunology, (September 1, 2002) Vol. 169, No. 5, pp. 2561-2569. http://www.jimmunol.org/. print.
ISSN: 0022-1767.
DT Article
LA English
AB The gene encoding **streptococcal** mitogenic exotoxin Z (**SMEZ**) was disrupted in **Streptococcus** pyogenes. Despite the presence of other **superantigen** genes, mitogenic responses in

human and murine HLA-DQ transgenic cells were abrogated when cells were stimulated with supernatant from the **smez**- mutant compared with the parent strain. Remarkably, disruption of **smez** led to a complete inability to elicit cytokine production (TNF-alpha, lymphotoxin-alpha, IFN-gamma, IL-1 and -8) from human cells, when cocultured with **streptococcal** supernatants. The potent effects of **SMEZ** were apparent even though transcription and expression of **SMEZ** were barely detectable. Human Vbeta8+ T cell proliferation in response to S. pyogenes was **SMEZ**-dependent. Cells from HLA-DQ8 transgenic mice were 3 logs more sensitive to **SMEZ**-13 than cells from HLA-DR1 transgenic or wild-type mice. In the mouse, **SMEZ** targeted the human Vbeta8+ TCR homologue, murine Vbeta11, at the expense of other TCR T cell subsets. Expression of **SMEZ** did not affect bacterial clearance or survival from peritoneal **streptococcal** infection in HLA-DQ8 mice, though effects of **SMEZ** on pharyngeal infection are unknown. Infection did lead to a rise in Vbeta11+ T cells in the spleen which was partly reversed by disruption of the **smez** gene. Most strikingly, a clear rise in murine Vbeta4+ cells was seen in mice infected with the **smez**- mutant S. pyogenes strain, indicating a potential role for **SMEZ** as a repressor of cognate anti-**streptococcal** responses.

L7 ANSWER 3 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 2001:345369 BIOSIS
DN PREV200100345369
TI Pyrogenicity and cytokine-inducing properties of **Streptococcus** pyogenes superantigens: Comparative study of **streptococcal** mitogenic exotoxin Z and pyrogenic exotoxin A.
AU Muller-Alouf, Heide; **Proft, Thomas**; Zollner, Thomas M.; Gerlach, Dieter; Champagne, Eric; Desreumaux, Pierre; Fitting, Catherine; Geoffroy-Fauvet, Christiane; Alouf, Joseph E.; Cavaillon, Jean-Marc (1)
CS (1) Department of Physiopathology, Institut Pasteur, 28 Rue Docteur Roux, 75015, Paris: jmcavail@pasteur.fr France
SO Infection and Immunity, (June, 2001) Vol. 69, No. 6, pp. 4141-4145. print. ISSN: 0019-9567.
DT Article
LA English
SL English
AB **Streptococcal** mitogenic exotoxin Z (**SMEZ**), a **superantigen** derived from **Streptococcus** pyogenes, provoked expansion of human lymphocytes expressing the Vbeta 2, 4, 7 and 8 motifs of T-cell receptor. **SMEZ** was pyrogenic in rabbits and stimulated the expression of the T-cell activation markers CD69 and cutaneous lymphocyte-associated antigen. A variety of cytokines was released by human mononuclear leukocytes stimulated with **SMEZ**, which was 10-fold more active than **streptococcal** pyrogenic exotoxin A. Th2-derived cytokines were elicited only by superantigens and not by **streptococcal** cells.

L7 ANSWER 4 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2002:188931 BIOSIS
DN PREV200200188931
TI Molecular analysis of the immunological role of **streptococcal** mitogenic exotoxin Z.
AU Unnikrishnan, M. (1); Altmann, D. (1); **Proft, T.**; Fraser, J. D.; Cohen, J. (1); Sriskandan, S. (1)
CS (1) Imperial College School of Medicine, London UK
SO Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 280. http://www.asmusa.org/mtgsrc/generalmeeting.htm. print.
Meeting Info.: 101st General Meeting of the American Society for Microbiology Orlando, FL, USA May 20-24, 2001

ISSN: 1060-2011.
DT Conference
LA English
AB **Streptococcal** mitogenic exotoxin Z is the most potent bacterial **superantigen** discovered to date. The biological function of **SMEZ** is unclear, but it may play a critical role in **streptococcal** pathogenesis; the gene is present in all strains studied and demonstrates extensive allelic variation. Aim: To characterize the immunological role of **SMEZ** in vitro and in vivo. Methods: **SmeZ** was insertionally inactivated in a clinical **Streptococcus** pyogenes strain, H293, to create strain H377. Proliferation of human PBMC, murine BALB/c, and HLA class II transgenic mouse splenocytes in response to purified rSMEZ, **SMEZ**+ and **SMEZ**-culture supernatants was measured by thymidine incorporation. Analysis of TCR Vbeta bearing T cell populations was performed by flow cytometry in human and murine cells. Mice were infected i.p. with either H293 or H377 and TCR Vbeta repertoire changes in spleen T cells were measured following infection. Results: Targeted disruption of **smeZ** was confirmed by Southern hybridisation and PCR. Despite the low level of expression of **SMEZ** in H293, disruption of **smeZ** led to a six-fold diminution of T cell proliferation in supernatant-stimulated human PBMC and a specific reduction in expansion of Vbeta8+ T cells. BALB/c mice splenocytes were poorly responsive to rSMEZ and did not proliferate in response to H293 or H377 supernatant. HLA-DQ transgenic murine spleen cells were highly responsive to rSMEZ compared with wild type and HLA-DR transgenic mice cells. HLA-DQ spleen cells were also highly responsive to H293 supernatant; proliferation was abolished by disruption of **smeZ** rSMEZ caused specific expansion of murine TCR Vbeta11+ (human TCR Vbeta8 gene homolog) T cells. In vivoexperiments demonstrated expansion of mTCR Vbeta11 cells following infection with H293 in spleen; this expansion was significantly reduced in mice infected with H377 in the spleen, confirming that **SMEZ** can cause a **superantigen** effect in vivo, in invasive murine **streptococcal** sepsis. Conclusion: We clearly demonstrate the potency and TCR Vbeta-specific effects of **SMEZ**. Our results suggest a definite role for this **superantigen** in **streptococcal** pathogenesis.

L7 ANSWER 5 OF 9 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 3
AN 2000-452370 [39] WPIDS
DNC C2000-137919
TI Novel superantigens from **streptococcus** pyogenes useful for genotyping **streptococcus** pyogenes clones expressing **SMEZ** -2 and for diagnosing a Kawasaki syndrome.
DC B04 D16
IN FRASER, J D; **PROFT, T**
PA (AUCK-N) AUCKLAND UNISERVICES LTD
CYC 91
PI WO 2000039159 A1 20000706 (200039)* EN 72p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000019010 A 20000731 (200050)
EP 1141000 A1 20011010 (200167) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2002535966 W 20021029 (200274) 89p
ADT WO 2000039159 A1 WO 1999-NZ228 19991224; AU 2000019010 A AU 2000-19010 19991224; EP 1141000 A1 EP 1999-962603 19991224, WO 1999-NZ228 19991224; JP 2002535966 W WO 1999-NZ228 19991224, JP 2000-591070 19991224

FDT AU 2000019010 A Based on WO 200039159; EP 1141000 A1 Based on WO 200039159; JP 2002535966 W Based on WO 200039159

PRAI NZ 1998-333589 19981224

AB WO 200039159 A UPAB: 20000818

NOVELTY - A **superantigen** (I) **SMEZ**-2, SPE-G, SPE-H or SPE-J, or its functionally equivalent variant, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) **SMEZ**-2, SPE-G, SPE-H, or SPE-J, having a 233, 234, 236, or 137 residue amino acid sequence, respectively, all fully defined in the specification;

(2) a polynucleotide (II) encoding (I), having a 702, 705, 711 or 414 nucleotide sequence, all fully defined in the specification, and encoding **SMEZ**-2, SPE-G, SPE-H, or SPE-J, respectively;

(3) a construct (III) comprising (I) and a cell-targeting molecule;

(4) a pharmaceutical composition comprising (III);

(5) an antibody (IV) which binds to (I);

(6) a nucleic acid molecule (V) which hybridizes to (II); and

(7) a kit which includes (II).

ACTIVITY - Cytostatic. No biological data given.

MECHANISM OF ACTION - T cell mitogens.

USE - (I) or (II) is used for subtyping **Streptococci** (claimed). They are also used for diagnosing a disease which is caused or mediated by expression of (I), in which the presence of (I) or (II) is detected by (IV) or (V), respectively, (claimed). The superantigens are used in diagnosis of disease such as Kawasaki syndrome. (II) can be used to design probes and primers for probing or amplifying parts of the **smez**-2, spe-g, spe-h, spe-j genes. They are also useful to recruit and activate T cells in a relatively non-specific fashion since they bind a large number of T cell receptor molecules by binding to the V beta domain. The constructs are useful in cancer therapy.

Dwg.0/13

L7 ANSWER 6 OF 9 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI

AN 2000-12141 BIOTECHDS

TI Novel superantigens from **Streptococcus** sp. pyogenes useful for genotyping **Streptococcus** pyogenes clones expressing **SMEZ**-2 and for diagnosing a Kawasaki syndrome; recombinant **superantigen** production and DNA probe, DNA primer and antibody for Kawasaki syndrome and disease diagnosis and therapy

AU Fraser J D; **Proft T**

PA Auckland-Uniservices

LO Auckland, New Zealand.

PI WO 2000039159 6 Jul 2000

AI WO 1999-NZ228 24 Dec 1999

PRAI NZ 1998-333589 24 Dec 1998

DT Patent

LA English

OS WPI: 2000-452370 [39]

AB A **Streptococcus** pyogenes **superantigen** (I) **SMEZ**-2, SPE-G, SPE-H or SPE-J, or its functionally equivalent variant, is claimed. Also claimed are: **SMEZ**-2, SPE-G, SPE-H or SPE-J, having a 233, 234, 236 or 137 amino acid protein sequence (specified), respectively; a DNA (II) encoding (I), having a 702, 705, 711 or 414 DNA sequence (specified), and encoding **SMEZ**-2, SPE-G, SPE-H or SPE-J, respectively; a construct (III) with (I) and a cell-targeting molecule; a pharmaceutical composition with (III); an antibody (IV) which binds to (I); a DNA probe (V) which hybridizes to (II); and a kit which has (II). (I) or (II) is used for subtyping **streptococci**. They are also used for diagnosing disease which is caused or mediated by expression of (I), in which the presence of (I) or (II) is detected by (IV) or (V), respectively. The superantigens are

used in diagnosis of disease such as Kawasaki syndrome. (II) can be used to design DNA probes and DNA primers for probing or amplifying parts of the **smez**-2, spe-g, spe-h, spe-j genes. They are also useful to recruit and activate T-lymphocytes in a relatively non-specific manner. The constructs are useful in cancer therapy. (72pp)

L7 ANSWER 7 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
AN 2000:293069 BIOSIS
DN PREV200000293069
TI The **streptococcal superantigen SMEZ** exhibits wide allelic variation, mosaic structure, and significant antigenic variation.
AU **Proft, Thomas**; Moffatt, S. Louise; Weller, Kylie D.; Paterson, A.; Martin, Diana; **Fraser, John D. (1)**
CS (1) Department of Molecular Medicine, School of Medicine, University of Auckland, Auckland New Zealand
SO Journal of Experimental Medicine, (May 15, 2000) Vol. 191, No. 10, pp. 1765-1776. print.
ISSN: 0022-1007.
DT Article
LA English
SL English
AB The frequencies of the newly identified **streptococcal superantigen** genes **smez**, spe-g, and spe-h were determined in a panel of 103 clinical isolates collected between 1976 and 1998 at various locations throughout New Zealand. **smez** and spe-g were found in every group A **Streptococcus** (GAS) isolate, suggesting a chromosomal location. The spe-h gene was found in only 24% of the GAS isolates and is probably located on a mobile DNA element. The **smez** gene displays extensive allelic variation and appears to be in linkage equilibrium with the M/emm type. 22 novel **smez** alleles were identified from 21 different M/emm types in addition to the already reported alleles **smez** and **smez**-2 with sequence identities between 94.5 and 99.9%. Three alleles are nonfunctional due to a single base pair deletion. The remaining 21 alleles encode distinct **SMEZ** variants. The mosaic structure of the **smez** gene suggests that this polymorphism has arisen from homologous recombination events rather than random point mutation. The recently resolved **SMEZ**-2 crystal structure shows that the polymorphic residues are mainly surface exposed and scattered over the entire protein. The allelic variation did not affect either Vbeta specificity or potency, but did result in significant antigenic differences. Neutralizing antibody responses of individual human sera against different **SMEZ** variants varied significantly. 98% of sera completely neutralized **SMEZ**-1, but only 85% neutralized **SMEZ**-2, a very potent variant that has not yet been found in any New Zealand isolate. **SMEZ**-specific Vbeta8 activity was found in culture supernatants of 66% of the GAS isolates, indicating a potential base for the development of a **SMEZ** targeting vaccine.

L7 ANSWER 8 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5
AN 2000:375574 BIOSIS
DN PREV200000375574
TI Conservation and variation in **superantigen** structure and activity highlighted by the three-dimensional structures of two new superantigens from **Streptococcus** pyogenes.
AU Arcus, Vickery L.; **Proft, Thomas**; Sigrell, Jill A.; Baker, Heather M.; **Fraser, John D.**; Baker, Edward N. (1)
CS (1) School of Biological Sciences, University of Auckland, Auckland New Zealand
SO Journal of Molecular Biology, (26 May, 2000) Vol. 299, No. 1, pp. 157-168. print.
ISSN: 0022-2836.

DT Article
LA English
SL English
AB Bacterial superantigens (SAgs) are a structurally related group of protein toxins secreted by Staphylococcus aureus and **Streptococcus** pyogenes. They are implicated in a range of human pathologies associated with bacterial infection whose symptoms result from SAg-mediated stimulation of a large number (2-20%) of T-cells. At the molecular level, bacterial SAgs bind to major histocompatability class II (MHC-II) molecules and disrupt the normal interaction between MHC-II and T-cell receptors (TCRs). We have determined high-resolution crystal structures of two newly identified **streptococcal** superantigens, SPE-H and **SMEZ**-2. Both structures conform to the generic bacterial **superantigen** folding pattern, comprising an OB-fold N-terminal domain and a beta-grasp C-terminal domain. SPE-H and **SMEZ**-2 also display very similar zinc-binding sites on the outer concave surfaces of their C-terminal domains. Structural comparisons with other SAgs identify two structural sub-families. Sub-families are related by conserved core residues and demarcated by variable binding surfaces for MHC-II and TCR. **SMEZ**-2 is most closely related to the **streptococcal** SAg SPE-C, and together they constitute one structural sub-family. In contrast, SPE-H appears to be a hybrid whose N-terminal domain is most closely related to the SEB sub-family and whose C-terminal domain is most closely related to the SPE-C/**SMEZ**-2 sub-family. MHC-II binding for both SPE-H and **SMEZ**-2 is mediated by the zinc ion at their C-terminal face, whereas the generic N-terminal domain MHC-II binding site found on many SAgs appears not to be present. Structural comparisons provide evidence for variations in TCR binding between SPE-H, **SMEZ** -2 and other members of the SAg family; the extreme potency of **SMEZ**-2 (active at 10-15 g ml-1 levels) is likely to be related to its TCR binding properties. The **smez** gene shows allelic variation that maps onto a considerable proportion of the protein surface. This allelic variation, coupled with the varied binding modes of SAgs to MHC-II and TCR, highlights the pressure on SAgs to avoid host immune defences.

L7 ANSWER 9 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 6
AN 1999:98436 BIOSIS
DN PREV199900098436
TI Identification and characterization of novel superantigens from **Streptococcus** pyogenes.
AU **Proft, Thomas** ; Moffatt, S. Louise; Berkahn, Celia J.; **Fraser, John D. (1)**
CS (1) Dep. Mol. Med., Sch. Med., Univ. Auckland, Private Bag 92019, Auckland New Zealand
SO Journal of Experimental Medicine, (Jan. 4, 1999) Vol. 189, No. 1, pp. 89-101.
ISSN: 0022-1007.
DT Article
LA English
AB Three novel **streptococcal superantigen** genes (spe-g, spe-h, and spe-j) were identified from the **Streptococcus** pyogenes M1 genomic database at the University of Oklahoma. A fourth novel gene (**smez**-2) was isolated from the S. pyogenes strain 2035, based on sequence homology to the **streptococcal** mitogenic exotoxin z (**smez**) gene. **SMEZ**-2, SPE-G, and SPE-J are most closely related to **SMEZ** and **streptococcal** pyrogenic exotoxin (SPE)-C, whereas SPE-H is most similar to the staphylococcal toxins than to any other **streptococcal** toxin. Recombinant (r)**SMEZ**, rSMEZ-2, rSPE-G, and rSPE-H were mitogenic for human peripheral blood lymphocytes with half-maximal responses between 0.02 and 50 pg/ml (rSMEZ-2 and rSPE-H, respectively). **SMEZ**-2 is the most potent **superantigen** (SAg) discovered thus far. All

toxins, except rSPE-G, were active on murine T cells, but with reduced potency. Binding to a human B-lymphoblastoid line was shown to be zinc dependent with high binding affinity of 15-65 nM. Evidence from modeled protein structures and competitive binding experiments suggest that high affinity binding of each toxin is to the major histocompatibility complex class II beta chain. Competition for binding between toxins was varied and revealed overlapping but discrete binding to subsets of class 11 molecules in the hierarchical order (**SMEZ**, SPE-C) > **SMEZ**-2 > SPE-H > SPE-G. The most common targets for the novel SAgs were human Vbeta2.1- and Vbeta4-expressing T cells. This might reflect a specific role for this subset of Vbetas in the immune defense of gram-positive bacteria.

```
=> s streptococc? mitogenic exotoxin
L8          30 STREPTOCOCC? MITOGENIC EXOTOXIN

=> s l8 and superantigen
L9          26 L8 AND SUPERANTIGEN

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10          10 DUP REM L9 (16 DUPLICATES REMOVED)

=> d bib ab 1-10

L10  ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2003 ACS
AN   2003:22707  CAPLUS
DN   138:88639
TI   Bacterial superantigen-antibody conjugates for treating human
     proliferative diseases or cancers
IN   Forsberg, Goeran; Erlandsson, Eva; Antonsson, Per; Walse, Bjoern
PA   Active Biotech AB, Swed.
SO   PCT Int. Appl., 102 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   WO 2003002143      A1   20030109      WO 2002-SE1188   20020619
         W:  AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES,
             FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
             MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK,
             SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW,
             AM, AZ, BY, KG
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 2003039655      A1   20030227      US 2001-900766   20010706
PRAI SE 2001-2327       A    20010628
AB   The present invention relates to compns. and methods of use, wherein the
     compn. comprises a conjugate of a bacterial superantigen and an
     antibody moiety.  More particularly, the bacterial superantigen
     has been modified to decrease seroreactivity with retained
     superantigen activity.  The bacterial superantigen is
     staphylococcal enterotoxin (SE), Streptococcus pyogenes exotoxin (SPE),
     Staphylococcus aureus toxic shock-syndrome toxin (TSST-1),
     streptococcal mitogenic exotoxin (SME) or
     superantigen (SSA), Staphylococcal enterotoxin A (SEA) or E (SEE).
     The antibody or active fragment is directed against a cancer-assocd. cell
```

surface structure. The **superantigen**-antibody conjugates are used for treating lung, breast, colon, kidney, pancreatic, ovarian, stomach, cervix and prostate cancer. The **superantigen**-antibody conjugates may optionally combine with cytokine such as interleukin esp. interleukin 2 for i.v. administration.
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 10 USPATFULL
AN 2003:57091 USPATFULL
TI Novel engineered **superantigen** for human therapy
IN Forsberg, Goran, Eslov, SWEDEN
Erlandsson, Eva, Dalby, SWEDEN
Antonsson, Per, Lund, SWEDEN
Walse, Bjorn, Lund, SWEDEN
PI US 2003039655 A1 20030227
AI US 2001-900766 A1 20010706 (9)
PRAI SE 2001-2327 20010628
DT Utility
FS APPLICATION
LREP FULBRIGHT & JAWORSKI L.L.P., Melissa W. Acosta, Suite 5100, 1301 McKinney, Houston, TX, 77010-3095
CLMN Number of Claims: 92
ECL Exemplary Claim: 1
DRWN 11 Drawing Page(s)
LN.CNT 2525
AB The present invention relates to compositions and methods of use, wherein the composition comprises a conjugate of a bacterial **superantigen** and an antibody moiety. More particularly, the bacterial **superantigen** has been modified to decrease seroreactivity with retained **superantigen** activity.

L10 ANSWER 3 OF 10 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 2002:513642 BIOSIS
DN PREV200200513642
TI The bacterial **superantigen streptococcal mitogenic exotoxin** Z is the major immunoactive agent of Streptococcus pyogenes.
AU Unnikrishnan, Meera; Altmann, Daniel M.; Proft, Thomas; Wahid, Faisal; Cohen, Jonathan; Fraser, John D.; Sriskandan, Shiranee (1)
CS (1) Department of Infectious Diseases, Faculty of Medicine, Hammersmith Hospital, Imperial College School of Science, Technology, and Medicine, Du Cane Road, London, W12 0NN: s.sriskandan@ic.ac.uk UK
SO Journal of Immunology, (September 1, 2002) Vol. 169, No. 5, pp. 2561-2569. http://www.jimmunol.org/. print.
ISSN: 0022-1767.
DT Article
LA English
AB The gene encoding **streptococcal mitogenic exotoxin** Z (SMEZ) was disrupted in Streptococcus pyogenes. Despite the presence of other **superantigen** genes, mitogenic responses in human and murine HLA-DQ transgenic cells were abrogated when cells were stimulated with supernatant from the smez- mutant compared with the parent strain. Remarkably, disruption of smez led to a complete inability to elicit cytokine production (TNF-alpha, lymphotoxin-alpha, IFN-gamma, IL-1 and -8) from human cells, when cocultured with streptococcal supernatants. The potent effects of SMEZ were apparent even though transcription and expression of SMEZ were barely detectable. Human Vbeta8+ T cell proliferation in response to S. pyogenes was SMEZ-dependent. Cells from HLA-DQ8 transgenic mice were 3 logs more sensitive to SMEZ-13 than cells from HLA-DR1 transgenic or wild-type mice. In the mouse, SMEZ targeted the human Vbeta8+ TCR homologue, murine Vbeta11, at the expense of other TCR T

cell subsets. Expression of SMEZ did not affect bacterial clearance or survival from peritoneal streptococcal infection in HLA-DQ8 mice, though effects of SMEZ on pharyngeal infection are unknown. Infection did lead to a rise in Vbeta11+ T cells in the spleen which was partly reversed by disruption of the smez gene. Most strikingly, a clear rise in murine Vbeta4+ cells was seen in mice infected with the smez- mutant S. pyogenes strain, indicating a potential role for SMEZ as a repressor of cognate anti-streptococcal responses.

L10 ANSWER 4 OF 10 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 2001:345369 BIOSIS
DN PREV200100345369
TI Pyrogenicity and cytokine-inducing properties of Streptococcus pyogenes superantigens: Comparative study of **streptococcal mitogenic exotoxin** Z and pyrogenic exotoxin A.
AU Muller-Alouf, Heide; Proft, Thomas; Zollner, Thomas M.; Gerlach, Dieter; Champagne, Eric; Desreumaux, Pierre; Fitting, Catherine; Geoffroy-Fauvet, Christiane; Alouf, Joseph E.; Cavaillon, Jean-Marc (1)
CS (1) Department of Physiopathology, Institut Pasteur, 28 Rue Docteur Roux, 75015, Paris: jmcavail@pasteur.fr France
SO Infection and Immunity, (June, 2001) Vol. 69, No. 6, pp. 4141-4145. print. ISSN: 0019-9567.
DT Article
LA English
SL English
AB **Streptococcal mitogenic exotoxin** Z (SMEZ), a **superantigen** derived from Streptococcus pyogenes, provoked expansion of human lymphocytes expressing the Vbeta 2, 4, 7 and 8 motifs of T-cell receptor. SMEZ was pyrogenic in rabbits and stimulated the expression of the T-cell activation markers CD69 and cutaneous lymphocyte-associated antigen. A variety of cytokines was released by human mononuclear leukocytes stimulated with SMEZ, which was 10-fold more active than streptococcal pyrogenic exotoxin A. Th2-derived cytokines were elicited only by superantigens and not by streptococcal cells.

L10 ANSWER 5 OF 10 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
AN 2001:195993 BIOSIS
DN PREV200100195993
TI Functional characterization of streptococcal pyrogenic exotoxin J, a novel **superantigen**.
AU McCormick, John K.; Pragman, Alexa A.; Stolpa, John C.; Leung, Donald Y. M.; Schlievert, Patrick M. (1)
CS (1) Department of Microbiology, University of Minnesota Medical School, 420 Delaware St., S.E, Minneapolis, MN, 55455: pats@lenti.med.umn.edu USA
SO Infection and Immunity, (March, 2001) Vol. 69, No. 3, pp. 1381-1388. print.
ISSN: 0019-9567.
DT Article
LA English
SL English
AB Streptococcal toxic syndrome (STSS) is a highly lethal, acute-onset illness that is a subset of invasive streptococcal disease. The majority of clinical STSS cases have been associated with the pyrogenic toxin superantigens (PTSAgs) streptococcal pyrogenic exotoxin A or C (SPE A or C), although cases have been reported that are not associated with either of these exotoxins. Recent genome sequencing projects have revealed a number of open reading frames that potentially encode proteins with similarity to SPEs A and C and to other PTSAgs. Here, we describe the cloning, expression, purification, and functional characterization of a novel exotoxin termed streptococcal pyrogenic exotoxin J (SPE J). Purified recombinant SPE J (rSPE J) expressed from Escherichia coli stimulated the

expansion of both rabbit splenocytes and human peripheral blood lymphocytes, preferentially expanded human T cells displaying Vbeta2, -3, -12, -14, and -17 on their T-cell receptors, and was active at concentrations as low as 5 X 10-6 mug/ml. Furthermore, rSPE J induced fevers in rabbits and was lethal in two models of STSS. Biochemically, SPE J had a predicted molecular weight of 24,444 and an isoelectric point of 7.7 and lacked the ability to form the cystine loop structure characteristic of many PTSAgs. SPE J shared 19.6, 47.1, 38.8, 18.1, 19.6, and 24.4% identify with SPEs A, C, G, and H, streptococcal **superantigen**, and **streptococcal mitogenic exotoxin** Z-2, respectively, and was immunologically cross-reactive with SPE C. The characterization of a seventh functional streptococcal PTSAg raises important questions relating to the evolution of the streptococcal superantigens.

L10 ANSWER 6 OF 10 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2002:293446 BIOSIS
DN PREV200200293446
TI Evidence for **superantigen** involvement in severe group A streptococcal tissue infections.
AU Norrby-Teglund, Anna (1); Thulin, Pontus; Gan, Bing S.; Kotb, Malak; McGeer, Allison; Andersson, Jan; Low, Donald E.
CS (1) Center for Infectious Medicine, Karolinska Institutet, Dept. of Medicine-I63, Huddinge University Hospital, SE-141 86, Stockholm: Anna.Norrby-Teglund@medhs.ki.se Sweden
SO Journal of Infectious Diseases, (1 October, 2001) Vol. 184, No. 7, pp. 853-860. print.
ISSN: 0022-1899.
DT Article
LA English
AB Host-pathogen interactions were studied in tissue biopsy samples from patients with severe invasive group A streptococcus (GAS) infections. Skin, subcutaneous tissue, and fascia biopsy samples were divided into clinical grade 1 (no evidence of inflammation (n = 7)) or clinical grade 2 (inflamed tissue-erythema and edema including cellulitis, fasciitis, and necrotizing fasciitis (n = 24)). In situ imaging demonstrated significantly higher bacterial load in biopsy samples of higher clinical grade ($P < .05$), and the bacterial load correlated with the in vivo expression of the **superantigen** streptococcal pyrogenic exotoxin F ($P < .02$). Increased expression of the interleukin-1 cytokines and significantly higher expression of tumor necrosis factor-beta, interferon-gamma, and the homing receptors CC chemokine receptor 5, CD44, and cutaneous lymphocyte-associated antigen ($P < .002$-$.05$) were observed in biopsy samples of higher clinical grade. Thus, the cytokine profile at the local site of infection mimics that of a typical **superantigen** cytokine response. The findings of this study demonstrate a critical role for superantigens and Th1 cytokines in GAS tissue infections.

L10 ANSWER 7 OF 10 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2002:188931 BIOSIS
DN PREV200200188931
TI Molecular analysis of the immunological role of **streptococcal mitogenic exotoxin** Z.
AU Unnikrishnan, M. (1); Altmann, D. (1); Proft, T.; Fraser, J. D.; Cohen, J. (1); Sriskandan, S. (1)
CS (1) Imperial College School of Medicine, London UK
SO Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 280. http://www.asmusa.org/mtgsrc/generalmeeting.htm. print.
Meeting Info.: 101st General Meeting of the American Society for Microbiology Orlando, FL, USA May 20-24, 2001
ISSN: 1060-2011.
DT Conference

LA English
AB **Streptococcal mitogenic exotoxin** Z is the most potent bacterial **superantigen** discovered to date. The biological function of SMEZ is unclear, but it may play a critical role in streptococcal pathogenesis; the gene is present in all strains studied and demonstrates extensive allelic variation. Aim: To characterize the immunological role of SMEZ in vitro and in vivo. Methods: SmeZ was insertionally inactivated in a clinical Streptococcus pyogenes strain, H293, to create strain H377. Proliferation of human PBMC, murine BALB/c, and HLA class II transgenic mouse splenocytes in response to purified rSMEZ, SMEZ+ and SMEZ-culture supernatants was measured by thymidine incorporation. Analysis of TCR Vbeta bearing T cell populations was performed by flow cytometry in human and murine cells. Mice were infected i.p. with either H293 or H377 and TCR Vbeta repertoire changes in spleen T cells were measured following infection. Results: Targeted disruption of smeZ was confirmed by Southern hybridisation and PCR. Despite the low level of expression of SMEZ in H293, disruption of smeZ led to a six-fold diminution of T cell proliferation in supernatant-stimulated human PBMC and a specific reduction in expansion of Vbeta8+ T cells. BALB/c mice splenocytes were poorly responsive to rSMEZ and did not proliferate in response to H293 or H377 supernatant. HLA-DQ transgenic murine spleen cells were highly responsive to rSMEZ compared with wild type and HLA-DR transgenic mice cells. HLA-DQ spleen cells were also highly responsive to H293 supernatant; proliferation was abolished by disruption of smeZ rSMEZ caused specific expansion of murine TCR Vbeta11+ (human TCR Vbeta8 gene homolog) T cells. In vivoexperiments demonstrated expansion of mTCR Vbeta11 cells following infection with H293 in spleen; this expansion was significantly reduced in mice infected with H377 in the spleen, confirming that SMEZ can cause a **superantigen** effect in vivo, in invasive murine streptococcal sepsis. Conclusion: We clearly demonstrate the potency and TCR Vbeta-specific effects of SMEZ. Our results suggest a definite role for this **superantigen** in streptococcal pathogenesis.

L10 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2003 ACS
AN 2000:455127 CAPLUS
DN 134:13824
TI Purification and biochemical characterization of a basic **superantigen** (SPEX/SMEZ3) from Streptococcus pyogenes
AU Gerlach, D.; Fleischer, B.; Wagner, M.; Schmidt, K.-H.; Vettermann, S.; Reichardt, W.
CS Institute of Medical Microbiology, Friedrich-Schiller-University Jena, Jena, D-07740, Germany
SO FEMS Microbiology Letters (2000), 188(2), 153-163
CODEN: FMLED7; ISSN: 0378-1097
PB Elsevier Science B.V.
DT Journal
LA English
AB A potent basic **superantigen** (designated streptococcal pyrogenic exotoxin X, SPEX/SMEZ3) was purified to homogeneity from culture supernatants of a Streptococcus pyogenes scarlatina strain of type 12 (genotype speA-, speC-) and characterized. Sequence alignments revealed SPEX to be an allele of the streptococcal mitogens type Z (SMEZ). The N-terminal amino acid sequence of SPEX was found with LEVDNNSLLR to be identical to the recently described acidic **superantigen** SMEZ. Although SPEX/SMEZ genes were present in all of the streptococcal strains tested, a toxin prodn. could only be detected in a small no. of strains. The produced toxin concn. in the culture supernatants of pos. strains differed between 0 and 20 ng ml-1. The purified SPEX stimulated human T-lymphocytes with V.beta.8 specificity at extremely low concns. (lower than 100 pg ml-1).
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 10 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
AN 1999:98436 BIOSIS
DN PREV199900098436
TI Identification and characterization of novel superantigens from Streptococcus pyogenes.
AU Proft, Thomas ; Moffatt, S. Louise; Berkahn, Celia J.; Fraser, John D. (1)
CS (1) Dep. Mol. Med., Sch. Med., Univ. Auckland, Private Bag 92019, Auckland New Zealand
SO Journal of Experimental Medicine, (Jan. 4, 1999) Vol. 189, No. 1, pp. 89-101.
ISSN: 0022-1007.
DT Article
LA English
AB Three novel streptococcal **superantigen** genes (spe-g, spe-h, and spe-j) were identified from the Streptococcus pyogenes M1 genomic database at the University of Oklahoma. A fourth novel gene (smez-2) was isolated from the S. pyogenes strain 2035, based on sequence homology to the **streptococcal mitogenic exotoxin** z (smez) gene. SMEZ-2, SPE-G, and SPE-J are most closely related to SMEZ and streptococcal pyrogenic exotoxin (SPE)-C, whereas SPE-H is most similar to the staphylococcal toxins than to any other streptococcal toxin. Recombinant (r)SMEZ, rSMEZ-2, rSPE-G, and rSPE-H were mitogenic for human peripheral blood lymphocytes with half-maximal responses between 0.02 and 50 pg/ml (rSMEZ-2 and rSPE-H, respectively). SMEZ-2 is the most potent **superantigen** (SAg) discovered thus far. All toxins, except rSPE-G, were active on murine T cells, but with reduced potency. Binding to a human B-lymphoblastoid line was shown to be zinc dependent with high binding affinity of 15-65 nM. Evidence from modeled protein structures and competitive binding experiments suggest that high affinity binding of each toxin is to the major histocompatibility complex class II beta chain. Competition for binding between toxins was varied and revealed overlapping but discrete binding to subsets of class 11 molecules in the hierarchical order (SMEZ, SPE-C) > SMEZ-2 > SPE-H > SPE-G. The most common targets for the novel SAgs were human Vbeta2.1- and Vbeta4-expressing T cells. This might reflect a specific role for this subset of Vbetas in the immune defense of gram-positive bacteria.

L10 ANSWER 10 OF 10 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 97286629 EMBASE
DN 1997286629
TI **Streptococcal mitogenic exotoxin** Z, a novel acidic superantigenic toxin produced by a T1 strain of Streptococcus pyogenes.
AU Kamezawa Y.; Nakahara T.; Nakano S.; Abe Y.; Nozaki-Renard J.; Isono T.
CS Y. Abe, Department of Pathology, Teikyo Univ. School of Medicine, Kaga 2-11-1, Itabashi-ku, Tokyo 173, Japan. a125025y@med.teikyo-u.ac.jp
SO Infection and Immunity, (1997) 65/9 (3828-3833).
Refs: 41
ISSN: 0019-9567 CODEN: INFIBR
CY United States
DT Journal; Article
FS 004 Microbiology
LA English
SL English
AB Streptococcus pyogenes T1 was previously found to produce an acidic mitogenic exotoxin, designated A.beta., antigenically distinct from erythrogenic toxin type A (ETA) of strains T1 and NY5. Following chemical analysis and biological characterization, we have renamed this toxin **streptococcal mitogenic exotoxin** Z (SMEZ). Physicochemical separation of SMEZ from ETA was successfully performed on a hydrophobic chromatograph. The isoelectric point was pH 5.3, and the

molecular size was estimated to be 28 kDa. These values were similar to those of ETA, but the amino acid composition and the NH2-terminal sequence of SMEZ were distinct from those of any mitogenic exotoxins hitherto described. Its mitogenic activity was found to be more potent than that of ETA in rabbit lymphocyte cultures. A specific antiserum raised against SMEZ did not cross- react with ETA, ETB, or ETC in the neutralization tests of mitogenic and erythrogenic activities. Its superantigenic nature was evident from the reverse transcriptase PCR findings of the T- cell receptor V.beta. profiles of rabbit lymphocytes stimulated in vitro. The V.beta. 8 subfamily was unique to SMEZ, while the V.beta. 2 and 6 subfamilies were found to be common among lymphocytes stimulated with ETA, ETB, ETC, or SMEZ. The results from this study provide an additional example of the diversity that exists among mitogenic or superantigenic exotoxins of streptococcal origin.

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     LIFESCI, CAPLUS, USPATFULL, USPAT2' ENTERED AT 15:41:51 ON 03 MAR 2003
                E PROFT THOMAS/AU
L1           86 S E1-E3
                E FRASER JOHN D/AU
L2           87 S E3-E5
L3          156 S L1 OR L2
L4           66 S L3 AND SUPERANTIGEN
L5           38 S L4 AND STREPTOCOCC?
L6           30 S L5 AND SMEZ?
L7            9 DUP REM L6 (21 DUPLICATES REMOVED)
L8           30 S STREPTOCOCC? MITOGENIC EXOTOXIN
L9           26 S L8 AND SUPERANTIGEN
L10          10 DUP REM L9 (16 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 15:48:25 ON 03 MAR 2003

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CA SUBSCRIBER PRICE                                     0.00      -1.30
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L11 9 DUP REM L6 (21 DUPLICATES REMOVED)

=> d bib ab 1-9

L11 ANSWER 1 OF 9 MEDLINE
AN 2003084097 IN-PROCESS
DN 22483693 PubMed ID: 12595453
TI Two novel superantigens found in both group a and group C **streptococcus**.
AU **Proft Thomas**; Webb Phillip D; Handley Vanessa; **Fraser John D**
CS Department of Molecular Medicine and Pathology, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand.
SO INFECTION AND IMMUNITY, (2003 Mar) 71 (3) 1361-9.
Journal code: 0246127. ISSN: 0019-9567.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030222
Last Updated on STN: 20030222
AB Two novel **streptococcal superantigen** genes (speL(Se) and speM(Se)) were identified from the **Streptococcus** equi genome database at the Sanger Center. Genotyping of 8 S. equi isolates and 40 **Streptococcus** pyogenes isolates resulted in the detection of the orthologous genes speL and speM in a restricted number of S. pyogenes isolates (15 and 5%, respectively). Surprisingly, the novel **superantigen** genes could not be found in any of the analyzed S. equi isolates. The results suggest that both genes are located on a mobile element that enables gene transfer between individual isolates and between **streptococci** from different Lancefield groups. S. equi pyrogenic exotoxin L (SPE-L(Se))/**streptococcal** pyrogenic exotoxin L (SPE-L) and SPE-M(Se)/SPE-M are most closely related to **SMEZ**, SPE-C, SPE-G, and SPE-J, but build a separate branch within this group. Recombinant SPE-L (rSPE-L) and rSPE-M were highly mitogenic for human peripheral blood lymphocytes, with half-maximum responses at 1 and 10 pg/ml, respectively. The results from competitive binding experiments suggest that both proteins bind major histocompatibility complex class II at the beta-chain, but not at the alpha-chain. The most common targets for both toxins were human Vbeta1.1 expressing T cells. Seroconversion against

SPE-L and SPE-M was observed in healthy blood donors, suggesting that the toxins are expressed in vivo. Interestingly, the speL gene is highly associated with S. pyogenes M89, a serotype that is linked to acute rheumatic fever in New Zealand.

L11 ANSWER 2 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 2002:513642 BIOSIS
DN PREV200200513642
TI The bacterial **superantigen streptococcal** mitogenic exotoxin Z is the major immunoactive agent of **Streptococcus** pyogenes.
AU Unnikrishnan, Meera; Altmann, Daniel M.; **Proft, Thomas**; Wahid, Faisal; Cohen, Jonathan; **Fraser, John D.**; Sriskandan, Shiranee (1)
CS (1) Department of Infectious Diseases, Faculty of Medicine, Hammersmith Hospital, Imperial College School of Science, Technology, and Medicine, Du Cane Road, London, W12 0NN: s.sriskandan@ic.ac.uk UK
SO Journal of Immunology, (September 1, 2002) Vol. 169, No. 5, pp. 2561-2569. http://www.jimmunol.org/. print.
ISSN: 0022-1767.
DT Article
LA English
AB The gene encoding **streptococcal** mitogenic exotoxin Z (**SMEZ**) was disrupted in **Streptococcus** pyogenes. Despite the presence of other **superantigen** genes, mitogenic responses in human and murine HLA-DQ transgenic cells were abrogated when cells were stimulated with supernatant from the **smez**- mutant compared with the parent strain. Remarkably, disruption of **smez** led to a complete inability to elicit cytokine production (TNF-alpha, lymphotoxin-alpha, IFN-gamma, IL-1 and -8) from human cells, when cocultured with **streptococcal** supernatants. The potent effects of **SMEZ** were apparent even though transcription and expression of **SMEZ** were barely detectable. Human Vbeta8+ T cell proliferation in response to S. pyogenes was **SMEZ**-dependent. Cells from HLA-DQ8 transgenic mice were 3 logs more sensitive to **SMEZ**-13 than cells from HLA-DR1 transgenic or wild-type mice. In the mouse, **SMEZ** targeted the human Vbeta8+ TCR homologue, murine Vbeta11, at the expense of other TCR T cell subsets. Expression of **SMEZ** did not affect bacterial clearance or survival from peritoneal **streptococcal** infection in HLA-DQ8 mice, though effects of **SMEZ** on pharyngeal infection are unknown. Infection did lead to a rise in Vbeta11+ T cells in the spleen which was partly reversed by disruption of the **smez** gene. Most strikingly, a clear rise in murine Vbeta4+ cells was seen in mice infected with the **smez**- mutant S. pyogenes strain, indicating a potential role for **SMEZ** as a repressor of cognate anti-**streptococcal** responses.

L11 ANSWER 3 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 2001:345369 BIOSIS
DN PREV200100345369
TI Pyrogenicity and cytokine-inducing properties of **Streptococcus** pyogenes superantigens: Comparative study of **streptococcal** mitogenic exotoxin Z and pyrogenic exotoxin A.
AU Muller-Alouf, Heide; **Proft, Thomas**; Zollner, Thomas M.; Gerlach, Dieter; Champagne, Eric; Desreumaux, Pierre; Fitting, Catherine; Geoffroy-Fauvet, Christiane; Alouf, Joseph E.; Cavaillon, Jean-Marc (1)
CS (1) Department of Physiopathology, Institut Pasteur, 28 Rue Docteur Roux, 75015, Paris: jmcavail@pasteur.fr France
SO Infection and Immunity, (June, 2001) Vol. 69, No. 6, pp. 4141-4145. print.
ISSN: 0019-9567.
DT Article
LA English

SL English
AB **Streptococcal** mitogenic exotoxin Z (**SMEZ**), a **superantigen** derived from **Streptococcus** pyogenes, provoked expansion of human lymphocytes expressing the Vbeta 2, 4, 7 and 8 motifs of T-cell receptor. **SMEZ** was pyrogenic in rabbits and stimulated the expression of the T-cell activation markers CD69 and cutaneous lymphocyte-associated antigen. A variety of cytokines was released by human mononuclear leukocytes stimulated with **SMEZ**, which was 10-fold more active than **streptococcal** pyrogenic exotoxin A. Th2-derived cytokines were elicited only by superantigens and not by **streptococcal** cells.

L11 ANSWER 4 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2002:188931 BIOSIS
DN PREV200200188931
TI Molecular analysis of the immunological role of **streptococcal** mitogenic exotoxin Z.
AU Unnikrishnan, M. (1); Altmann, D. (1); **Proft, T.**; Fraser, J. D.; Cohen, J. (1); Sriskandan, S. (1)
CS (1) Imperial College School of Medicine, London UK
SO Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 280. http://www.asmusa.org/mtgsrc/generalmeeting.htm. print.
Meeting Info.: 101st General Meeting of the American Society for Microbiology Orlando, FL, USA May 20-24, 2001
ISSN: 1060-2011.
DT Conference
LA English
AB **Streptococcal** mitogenic exotoxin Z is the most potent bacterial **superantigen** discovered to date. The biological function of **SMEZ** is unclear, but it may play a critical role in **streptococcal** pathogenesis; the gene is present in all strains studied and demonstrates extensive allelic variation. Aim: To characterize the immunological role of **SMEZ** in vitro and in vivo. Methods: **SmeZ** was insertionally inactivated in a clinical **Streptococcus** pyogenes strain, H293, to create strain H377. Proliferation of human PBMC, murine BALB/c, and HLA class II transgenic mouse splenocytes in response to purified rSMEZ, **SMEZ**+ and **SMEZ**-culture supernatants was measured by thymidine incorporation. Analysis of TCR Vbeta bearing T cell populations was performed by flow cytometry in human and murine cells. Mice were infected i.p. with either H293 or H377 and TCR Vbeta repertoire changes in spleen T cells were measured following infection. Results: Targeted disruption of **smeZ** was confirmed by Southern hybridisation and PCR. Despite the low level of expression of **SMEZ** in H293, disruption of **smeZ** led to a six-fold diminution of T cell proliferation in supernatant-stimulated human PBMC and a specific reduction in expansion of Vbeta8+ T cells. BALB/c mice splenocytes were poorly responsive to rSMEZ and did not proliferate in response to H293 or H377 supernatant. HLA-DQ transgenic murine spleen cells were highly responsive to rSMEZ compared with wild type and HLA-DR transgenic mice cells. HLA-DQ spleen cells were also highly responsive to H293 supernatant; proliferation was abolished by disruption of **smeZ** rSMEZ caused specific expansion of murine TCR Vbeta11+ (human TCR Vbeta8 gene homolog) T cells. In vivoexperiments demonstrated expansion of mTCR Vbeta11 cells following infection with H293 in spleen; this expansion was significantly reduced in mice infected with H377 in the spleen, confirming that **SMEZ** can cause a **superantigen** effect in vivo, in invasive murine **streptococcal** sepsis. Conclusion: We clearly demonstrate the potency and TCR Vbeta-specific effects of **SMEZ**. Our results suggest a definite role for this **superantigen** in **streptococcal** pathogenesis.

L11 ANSWER 5 OF 9 WPIDS (C) 2003 THOMSON DERWENT DUPLICATE 3
AN 2000-452370 [39] WPIDS
DNC C2000-137919
TI Novel superantigens from **streptococcus** pyogenes useful for genotyping **streptococcus** pyogenes clones expressing **SMEZ** -2 and for diagnosing a Kawasaki syndrome.
DC B04 D16
IN FRASER, J D; **PROFT, T**
PA (AUCK-N) AUCKLAND UNISERVICES LTD
CYC 91
PI WO 2000039159 A1 20000706 (200039)* EN 72p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000019010 A 20000731 (200050)
EP 1141000 A1 20011010 (200167) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2002535966 W 20021029 (200274) 89p
ADT WO 2000039159 A1 WO 1999-NZ228 19991224; AU 2000019010 A AU 2000-19010 19991224; EP 1141000 A1 EP 1999-962603 19991224, WO 1999-NZ228 19991224; JP 2002535966 W WO 1999-NZ228 19991224, JP 2000-591070 19991224
FDT AU 2000019010 A Based on WO 200039159; EP 1141000 A1 Based on WO 200039159; JP 2002535966 W Based on WO 200039159
PRAI NZ 1998-333589 19981224
AB WO 200039159 A UPAB: 20000818
NOVELTY - A **superantigen** (I) **SMEZ**-2, SPE-G, SPE-H or SPE-J, or its functionally equivalent variant, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) **SMEZ**-2, SPE-G, SPE-H, or SPE-J, having a 233, 234, 236, or 137 residue amino acid sequence, respectively, all fully defined in the specification;
(2) a polynucleotide (II) encoding (I), having a 702, 705, 711 or 414 nucleotide sequence, all fully defined in the specification, and encoding **SMEZ**-2, SPE-G, SPE-H, or SPE-J, respectively;
(3) a construct (III) comprising (I) and a cell-targeting molecule;
(4) a pharmaceutical composition comprising (III);
(5) an antibody (IV) which binds to (I);
(6) a nucleic acid molecule (V) which hybridizes to (II); and
(7) a kit which includes (II).
ACTIVITY - Cytostatic. No biological data given.
MECHANISM OF ACTION - T cell mitogens.
USE - (I) or (II) is used for subtyping **Streptococci** (claimed). They are also used for diagnosing a disease which is caused or mediated by expression of (I), in which the presence of (I) or (II) is detected by (IV) or (V), respectively, (claimed). The superantigens are used in diagnosis of disease such as Kawasaki syndrome. (II) can be used to design probes and primers for probing or amplifying parts of the **smez**-2, spe-g, spe-h, spe-j genes. They are also useful to recruit and activate T cells in a relatively non-specific fashion since they bind a large number of T cell receptor molecules by binding to the V beta domain. The constructs are useful in cancer therapy.
Dwg.0/13

L11 ANSWER 6 OF 9 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
AN 2000-12141 BIOTECHDS
TI Novel superantigens from **Streptococcus** sp. pyogenes useful for genotyping **Streptococcus** pyogenes clones expressing **SMEZ**-2 and for diagnosing a Kawasaki syndrome;

recombinant **superantigen** production and DNA probe, DNA primer and antibody for Kawasaki syndrome and disease diagnosis and therapy

AU Fraser J D; **Proft T**
PA Auckland-Uniservices
LO Auckland, New Zealand.
PI WO 2000039159 6 Jul 2000
AI WO 1999-NZ228 24 Dec 1999
PRAI NZ 1998-333589 24 Dec 1998
DT Patent
LA English
OS WPI: 2000-452370 [39]
AB A **Streptococcus** pyogenes **superantigen** (I) **SMEZ**-2, SPE-G, SPE-H or SPE-J, or its functionally equivalent variant, is claimed. Also claimed are: **SMEZ**-2, SPE-G, SPE-H or SPE-J, having a 233, 234, 236 or 137 amino acid protein sequence (specified), respectively; a DNA (II) encoding (I), having a 702, 705, 711 or 414 DNA sequence (specified), and encoding **SMEZ**-2, SPE-G, SPE-H or SPE-J, respectively; a construct (III) with (I) and a cell-targeting molecule; a pharmaceutical composition with (III); an antibody (IV) which binds to (I); a DNA probe (V) which hybridizes to (II); and a kit which has (II). (I) or (II) is used for subtyping **streptococci**. They are also used for diagnosing disease which is caused or mediated by expression of (I), in which the presence of (I) or (II) is detected by (IV) or (V), respectively. The superantigens are used in diagnosis of disease such as Kawasaki syndrome. (II) can be used to design DNA probes and DNA primers for probing or amplifying parts of the **smez**-2, spe-g, spe-h, spe-j genes. They are also useful to recruit and activate T-lymphocytes in a relatively non-specific manner. The constructs are useful in cancer therapy. (72pp)

L11 ANSWER 7 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
AN 2000:293069 BIOSIS
DN PREV200000293069
TI The **streptococcal superantigen SMEZ** exhibits wide allelic variation, mosaic structure, and significant antigenic variation.
AU **Proft, Thomas**; Moffatt, S. Louise; Weller, Kylie D.; Paterson, A.; Martin, Diana; **Fraser, John D. (1)**
CS (1) Department of Molecular Medicine, School of Medicine, University of Auckland, Auckland New Zealand
SO Journal of Experimental Medicine, (May 15, 2000) Vol. 191, No. 10, pp. 1765-1776. print.
ISSN: 0022-1007.
DT Article
LA English
SL English
AB The frequencies of the newly identified **streptococcal superantigen** genes **smez**, spe-g, and spe-h were determined in a panel of 103 clinical isolates collected between 1976 and 1998 at various locations throughout New Zealand. **smez** and spe-g were found in every group A **Streptococcus** (GAS) isolate, suggesting a chromosomal location. The spe-h gene was found in only 24% of the GAS isolates and is probably located on a mobile DNA element. The **smez** gene displays extensive allelic variation and appears to be in linkage equilibrium with the M/emm type. 22 novel **smez** alleles were identified from 21 different M/emm types in addition to the already reported alleles **smez** and **smez**-2 with sequence identities between 94.5 and 99.9%. Three alleles are nonfunctional due to a single base pair deletion. The remaining 21 alleles encode distinct **SMEZ** variants. The mosaic structure of the **smez** gene suggests that this polymorphism has arisen from homologous recombination events rather than random point mutation. The recently resolved

SMEZ-2 crystal structure shows that the polymorphic residues are mainly surface exposed and scattered over the entire protein. The allelic variation did not affect either Vbeta specificity or potency, but did result in significant antigenic differences. Neutralizing antibody responses of individual human sera against different **SMEZ** variants varied significantly. 98% of sera completely neutralized **SMEZ**-1, but only 85% neutralized **SMEZ**-2, a very potent variant that has not yet been found in any New Zealand isolate. **SMEZ**-specific Vbeta8 activity was found in culture supernatants of 66% of the GAS isolates, indicating a potential base for the development of a **SMEZ** targeting vaccine.

L11 ANSWER 8 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5
AN 2000:375574 BIOSIS
DN PREV200000375574
TI Conservation and variation in **superantigen** structure and activity highlighted by the three-dimensional structures of two new superantigens from **Streptococcus** pyogenes.
AU Arcus, Vickery L.; **Proft, Thomas**; Sigrell, Jill A.; Baker, Heather M.; **Fraser, John D.**; Baker, Edward N. (1)
CS (1) School of Biological Sciences, University of Auckland, Auckland New Zealand
SO Journal of Molecular Biology, (26 May, 2000) Vol. 299, No. 1, pp. 157-168. print.
ISSN: 0022-2836.
DT Article
LA English
SL English
AB Bacterial superantigens (SAgs) are a structurally related group of protein toxins secreted by Staphylococcus aureus and **Streptococcus** pyogenes. They are implicated in a range of human pathologies associated with bacterial infection whose symptoms result from SAg-mediated stimulation of a large number (2-20%) of T-cells. At the molecular level, bacterial SAgs bind to major histocompatability class II (MHC-II) molecules and disrupt the normal interaction between MHC-II and T-cell receptors (TCRs). We have determined high-resolution crystal structures of two newly identified **streptococcal** superantigens, SPE-H and **SMEZ**-2. Both structures conform to the generic bacterial **superantigen** folding pattern, comprising an OB-fold N-terminal domain and a beta-grasp C-terminal domain. SPE-H and **SMEZ**-2 also display very similar zinc-binding sites on the outer concave surfaces of their C-terminal domains. Structural comparisons with other SAgs identify two structural sub-families. Sub-families are related by conserved core residues and demarcated by variable binding surfaces for MHC-II and TCR. **SMEZ**-2 is most closely related to the **streptococcal** SAg SPE-C, and together they constitute one structural sub-family. In contrast, SPE-H appears to be a hybrid whose N-terminal domain is most closely related to the SEB sub-family and whose C-terminal domain is most closely related to the SPE-C/**SMEZ**-2 sub-family. MHC-II binding for both SPE-H and **SMEZ**-2 is mediated by the zinc ion at their C-terminal face, whereas the generic N-terminal domain MHC-II binding site found on many SAgs appears not to be present. Structural comparisons provide evidence for variations in TCR binding between SPE-H, **SMEZ** -2 and other members of the SAg family; the extreme potency of **SMEZ**-2 (active at 10-15 g ml-1 levels) is likely to be related to its TCR binding properties. The **smez** gene shows allelic variation that maps onto a considerable proportion of the protein surface. This allelic variation, coupled with the varied binding modes of SAgs to MHC-II and TCR, highlights the pressure on SAgs to avoid host immune defences.

L11 ANSWER 9 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 6
AN 1999:98436 BIOSIS

DN PREV199900098436
TI Identification and characterization of novel superantigens from **Streptococcus** pyogenes.
AU **Proft, Thomas** ; Moffatt, S. Louise; Berkahn, Celia J.; **Fraser, John D. (1)**
CS (1) Dep. Mol. Med., Sch. Med., Univ. Auckland, Private Bag 92019, Auckland New Zealand
SO Journal of Experimental Medicine, (Jan. 4, 1999) Vol. 189, No. 1, pp. 89-101.
ISSN: 0022-1007.
DT Article
LA English
AB Three novel **streptococcal superantigen** genes (spe-g, spe-h, and spe-j) were identified from the **Streptococcus** pyogenes M1 genomic database at the University of Oklahoma. A fourth novel gene (**smez**-2) was isolated from the S. pyogenes strain 2035, based on sequence homology to the **streptococcal** mitogenic exotoxin z (**smez**) gene. **SMEZ**-2, SPE-G, and SPE-J are most closely related to **SMEZ** and **streptococcal** pyrogenic exotoxin (SPE)-C, whereas SPE-H is most similar to the staphylococcal toxins than to any other **streptococcal** toxin. Recombinant (r)**SMEZ**, rSMEZ-2, rSPE-G, and rSPE-H were mitogenic for human peripheral blood lymphocytes with half-maximal responses between 0.02 and 50 pg/ml (rSMEZ-2 and rSPE-H, respectively). **SMEZ**-2 is the most potent **superantigen** (SAg) discovered thus far. All toxins, except rSPE-G, were active on murine T cells, but with reduced potency. Binding to a human B-lymphoblastoid line was shown to be zinc dependent with high binding affinity of 15-65 nM. Evidence from modeled protein structures and competitive binding experiments suggest that high affinity binding of each toxin is to the major histocompatibility complex class II beta chain. Competition for binding between toxins was varied and revealed overlapping but discrete binding to subsets of class 11 molecules in the hierarchical order (**SMEZ**, SPE-C) > **SMEZ**-2 > SPE-H > SPE-G. The most common targets for the novel SAgs were human Vbeta2.1- and Vbeta4-expressing T cells. This might reflect a specific role for this subset of Vbetas in the immune defense of gram-positive bacteria.

WEST Search History

DATE: Monday, March 03, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=ADJ			
L32	bacteria 5 adj superantigen	0	L32
L31	bacteria 5 adj earth	0	L31
L30	bacteria 5 adj earth	0	L30
L29	bacteri? 10Adj superantigen?	0	L29
L28	superantigen and Smez?2	1	L28
L27	proft-thomas.in.	0	L27
L26	proft-thomas.in.	0	L26
L25	fraser-john-d.in.	14	L25
L24	(bacteria 5 adj superantigen) AnD ((@pd > 20030227)!)	0	L24
L23	(bacteria 5 adj earth) AnD ((@pd > 20030227)!)	0	L23
L22	(bacteria 5 adj earth) AnD ((@pd > 20030227)!)	0	L22
L21	(bacteri? 10Adj superantigen?) AnD ((@pd > 20030227)!)	0	L21
L20	(superantigen and Smez?2) AnD ((@pd > 20030227)!)	0	L20
L19	(proft-thomas.in.) AnD ((@pd > 20030227)!)	0	L19
L18	bacteria 5 adj superantigen	0	L18
L17	(proft-thomas.in.) AnD ((@pd > 20030227)!)	0	L17
L16	bacteria 5 adj earth	0	L16
L15	(fraser-john-d.in.) AnD ((@pd > 20030227)!)	0	L15
L14	bacteria 5 adj earth	0	L14
L13	bacteri? 10Adj superantigen?	0	L13
L12	superantigen and Smez?2	1	L12
L11	bacteria 5 adj superantigen	0	L11
L10	proft-thomas.in.	0	L10
L9	bacteria 5 adj earth	0	L9
L8	proft-thomas.in.	0	L8
L7	fraser-john-d.in.	14	L7
L6	bacteria 5 adj earth	0	L6
L5	bacteri? 10Adj superantigen?	0	L5
L4	superantigen and Smez?2	1	L4
L3	proft-thomas.in.	0	L3
L2	proft-thomas.in.	0	L2
L1	fraser-john-d.in.	14	L1

END OF SEARCH HISTORY

Streptococcal mitogenic exotoxin Z